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(54) Title: METHOD AND COMPOSITION FOR TREATING AND PREVENTING DRY SKIN DISORDERS

(57) Abstract

A method and composition for treating and preventing dry skin includes a lipid concentrate blended from a combination of the three naturally-occurring lipid groups found in the stratum corneum. The concentrate may be applied topically as prepared, or may be blended with a therapeutically acceptable vehicle suitable for topical application.

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METHOD AND COMPOSITION FOR TREATING AND PREVENTING DRY SKIN DISORDERS

This invention relates generally to dermatological preparations and, more particularly, to methods and compositions for treating and preventing dry skin.

Background of the Invention

Dry skin, also known as xerosis or asteatosis affects millions of Americans each year. Attempts to treat or prevent dry skin have led to the development of a large assortment of skin creams and lotions. All of these creams and lotions have been developed from either the point of view that applying an occlusive lipid such as petrolatum or mineral oil can retard moisture loss from the skin, or that the incorporation of water-soluble materials, such as free amino acids, organic acids, inorganic ions or urea, into the cream, ointment, gel or lotion can trap or retain water in the skin.

It has been demonstrated over the last few years that the stratum corneum of the skin contains certain lipids which may form complicated layers within the stratum corneum thus forming a "water barrier" which prevents water loss from the skin. It has been discovered that formulations may be prepared composed of components of the skin's natural water barrier forming lipid complex and that when these formulations are used by themselves or when they are incorporated into creams, ointments, gels and lotions, the resulting products provide unsurpassed protection against and treatment for dry skin conditions.

In preparing the formulations disclosed herein, combinations of components from three separate classes of stratum corneum lipids were utilized: (1) free fatty acids; (2) sterols and sterol esters; and (3) phospholipids and glycolipids.

Summary of the Invention

The present invention provides an improved method and composition for prophylaxis for or treatment of dry skin, consisting of preparing a formulation composed of representative lipids from the three classes of lipids naturally found in the stratum corneum. Such a formulation may be applied directly or may be incorporated into a cream, ointment, gel or lotion and the resulting product applied in order to prevent or treat dryness of the skin.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

While other lipids may be utilized, the following members of the three stratum corneum lipid classes combined under this invention have been successfully utilized:

1. Fatty acids: arachidonic, linoleic, linolenic, palmitic, stearic, oleic and docosanoic;
2. Sterols and sterol esters: cholesterol and cholesterol sulfate; and
3. Phospholipids and glycolipids: ceramides and lecithin.

The proportions of the three classes vary in selected lipid concentrate formulations but generally fall within the following ranges:

Fatty acids: 25 to 75%

Sterols and sterol esters: 10 to 40%

Phospholipids and glycolipids: 5 to 40%

The resulting lipid concentrate formulation may then be added to cream, ointment, gel or lotion vehicles in weight/weight concentrations ranging from about 1% to about 50%. The following examples further illustrate the invention:

A therapeutic skin formula to treat and prevent dry skin was formulated by adding 15 gm of a lipid concentrate composed of 30% W/W cholesterol (obtained under the trade designation Loralan- CH from the Lanaetex Products, Inc., Elizabeth, New Jersey), 20% W/W lecithin [obtained from American Lecithin Company, Inc., Atlanta Georgia), and 50% W/W of a mixture of linoleic acid, linolenic acid and arachidonic acid (obtained under the trade designation of EFA complex from Phillip Rockley, Ltd., New York, New York) to a lotion base as follows:

Isopropyl Myristate	5.0%	7.5 gm
Cetyl Alcohol	2.0%	3.0 gm
Glyceryl Stearate and PEG-100 Stearate (Arlacel 165)	5.0%	7.5 gm
Benzyl Alcohol	1.0%	1.5 gm
Lipid Concentrate	10.0%	15.0 gm
70% Sorbitol solution	25.0%	37.5 gm
Distilled Water	52.0%	78.0 gm
TOTAL	100.0%	150.0 gm

This formulation was applied to the dry skin of a 44 year old male and produced noticeably softer more supple skin after only one application.

Example 2

A therapeutic moisturizing formulation was prepared consisting of a lipid concentrate containing 10 ml of linoleic acid (obtained from Emery Industries, Cincinnati, Ohio), 10 ml linolenic acid (obtained from Fluka Chemical Corporation, Ronkonkoma, New York), 10 gm of a mixture of lecithin, cephalin and lipositol (obtained under the trade designation of Asolectin from Fluka Chemical Corporation, Ronkonkoma, New York), and 10 gm of cholesterol (obtained under the trade designation of Loralan- CH from the Lanaetex Products,

Inc., Elizabeth, New Jersey). The resulting mixture was blended to make a cream composed as follows:

Isopropyl Myristate	5.0%	7.5 gm
Cetyl Alcohol	3.0%	4.5 gm
Glyceryl stearate and PEG -100 stearate (Arlacel 165)	5.0%	7.5 gm
Benzyl Alcohol	1.0%	1.5 gm
Lipid Concentrate	5.0%	7.5 gm
70% Sorbitol solution	25.0%	37.5 gm
Distilled Water	56.0%	84.0 gm
TOTAL	100.0%	150.0 gm

This formulation was applied to the very dry skin on the lower legs of a 43 year old woman. Within 24 hours of twice daily application the treated skin was noticeably softer, more moist and supple.

Tests were also performed to assess the efficacy of the present invention in preventing water loss. Baseline measurements of 15 healthy adult test subjects were performed to determine the barrier-forming properties of different formulations of the present invention, and to compare these properties with those of two commercially-available skin creams, Eucerin*, manufactured by Beiersdorf, Inc., Norwalk, Connecicut, and Moisturel*, manufactured by Westwood Pharmaceuticals, Inc. Buffalo, N.Y.. A Servo Med Evaporimeter was used to measure rate of water loss from a 4.9 cm^2* patch of unprotected skin. Thereafter, formulations of the present invention were applied to the test subjects at separate 4.9 cm^2* test sites, as were applications of Eucerin* and Moisturel* skin creams. Each application consisted of 25 microliters of each formulation.

Lipid Concentrate I consisted of 30% w/w of cholesterol, 20% w/w of lecithin and ceramides, and 50% w/w of the linoleic, linolenic and arachidonic acid mix.

Lipid Concentrate II consisted of 15% w/w of cholesterol, 10% w/w lecithin and ceramides, and 75% w/w of the linoleic, linolenic and arachidonic acid mix.

The formulations tested were prepared as follows:

FORMULA 1

	Percent by Weight
Isopropyl Myristate	5.0
Cetyl Alcohol	3.0
Arlacel 165	5.0
Benzyl Alcohol	1.0
Lipid Concentrate II	10.0
70% Sorbitol Solution	25.0
Distilled Water	51.0
TOTAL	100.0

FORMULA 2

	Percent by Weight
Isopropyl Myristate	5.0
Cetyl Alcohol	3.0
Arlacel 165	5.0
Benzyl Alcohol	1.0
Lipid Concentrate II	5.0
70% Sorbitol Solution	25.0
Distilled Water	56.0
TOTAL	100.0

FORMULA 3

	Percent by Weight
Isopropyl Myristate	5.0
Cetyl Alcohol	3.0
Arlacel 165	5.0
Benzyl Alcohol	1.0
Lipid Concentrate I	10.0
Vitamin E	1.0
70% Sorbitol Solution	25.0
Distilled Water	50.0
TOTAL	100.0

Water loss measurements showed that all five formulations tested reduced water loss as compared to the untreated site, with the formulations of the present invention establishing a stronger barrier to water loss than the commercially available preparations. The test results were as follows:

	% change in evaporative water loss
Formula 1	3.4
Formula 2	3.5
Formula 3	3.6
Eucerin^{R}	3.7
Moisturel^{R}	3.9
Untreated Site	4.5

While the foregoing has presented specific embodiments of the present invention, it is to be understood that these embodiments have been presented by way of example only. It is expected that others will perceive variations which, while varying from the foregoing, do not depart from the spirit and scope of the invention as herein described and claimed. None of the foregoing is attempted to in any manner limit the scope of the present invention.

What is claimed is:

1. A method for prophylaxis or treatment of dry skin, said method comprising topical application to the skin of a concentrate of one or more constituents from each of the three classes of naturally-occurring stratum corneum lipids.

2. The method of Claim 1 wherein said three classes of lipids are fatty acids, sterol and sterol esters, and phospholipids and glycolipids.

3. The method of Claim 2 wherein said fatty acid is selected as one or more of the following: arachidonic acid, linoleic acid, linolenic acid, palmitic acid, stearic acid, oleic acid and docosanoic acid.

4. The method of Claim 2 wherein said sterol and/or sterol ester is selected from the group consisting of cholesterol and cholesterol sulfate.

5. The method of Claim 2 wherein said phospholipids and/or glycolipids are selected from the group consisting of ceramides and lecithin.

6. The method of in Claim 2 wherein said lipids are present in said concentrate in the following concentrations: fatty acids about 25% to about 75% by weight; sterols and sterol esters about 10% to about %40 by weight; and phospholipids and glycolipids about 5% to about 40% by weight.

7. The method of Claim 2 including the step of incorporating said concentrate into a pharmaceutically acceptable vehicle for topical application.

8. The method of Claim 7 wherein said vehicle is a cream, a gel, a lotion or an ointment.

9. A lipid concentrate for the prophylaxis and treatment of dry skin, said concentrate comprising at least one constituent from each of the following groups of naturally-occurring stratum corneum lipids: fatty acids, sterols and sterol esters, and phospholipids and glycolipids.

10. The concentrate of Claim 9 wherein said fatty acids are present in a proportion of about 25% to about 75% by weight, said sterol and sterol esters are present in a proportion of about 10% to about 40% by weight, and said phospholipids and glycolipids are present in a proportion from about 5% to about 40% by weight.

11. The concentrate of Claim 9, wherein said fatty acid is selected as one or more of the following: arachidonic acid, linoleic acid, linolenic acid palmitic acid, stearic acid oleic acid and docosanoic acid.

12. The concentrate of Claim 9 wherein said sterol and sterol ester is selected from the group comprising of cholesterol and cholesterol sulfate.

13. The concentrate of Claim 9 wherein said phospholipids and glycolipids are selected from the group comprising ceramides and lecithin.

14. The concentrate of Claim 9 including a pharmaceutically acceptable vehicle suitable for topical application of said concentrate.

15. The composition of Claim 14 wherein said vehicle is selected from the group of creams, gels, lotions and ointments.

16. The composition of Claim 14 comprising the following constituents, by weight:

Isopropyl Myristate	about	5.0%
Cetyl Alcohol	about	2.0%
Glyceryl stearate and PEG -100 stearate (Arlacel 165)	about	5.0%
Benzyl Alcohol	about	1.0%
Lipid Concentrate	about	10.0%
70% Sorbitol solution	about	25.0%
Distilled Water	about	52.0%

17. The composition of Claim 16 wherein said lipid concentrate comprises, by weight, 30% cholesterol,

20% lecithin and 50% of a mixture of linoleic acid, linolenic acid and arachidonic acid.

18. The composition of Claim 14 comprising the following constituents, by weight:

Isopropyl Myristate	about	5.0%
Cetyl Alcohol	about	3.0%
Glyceryl stearate and PEG -100 stearate (Arlacel 165)	about	5.0%
Benzyl Alcohol	about	1.0%
Lipid Concentrate	about	5.0%
70% Sorbitol solution	about	25.0%
Distilled Water	about	56.0%

19. The composition of Claim 18 wherein said lipid concentrate comprises about 10ml of linoleic acid, about 10 ml. of linolenic acid, about 10 gm of a mixture of lecithin, cephalin and liposital, and about 10 gm of cholesterol.

20. The composition of Claim 14 comprising the following constituents by weight:

Isopropyl Myristate	about	5.0%
Cetyl Alcohol	about	3.0%
Arlacel 165	about	5.0%
Benzyl Alcohol	about	1.0%
Lipid Concentrate	about	10.0%
70% Sorbitol Solution	about	25.0%
Distilled Water	about	51.0%

21. The composition of Claim 20 wherein said lipid concentrate comprises, by weight, about 15% cholesterol, about 10% lecithin and ceramides, and about 75% linoleic, Iinolenic and arachidonic acids.

22. The composition of Claim 14 comprising the following constituents, by weight:

Isopropyl Myristate	about	5.0%
Cetyl Alcohol	about	3.0%
Arlacel 165	about	5.0%
Benzyl Alcohol	about	1.0%
Lipid Concentrate	about	5.0%
70% Sorbitol Solution	about	25.0%
Distilled Water	about	56.0%

23. The composition of Claim 22 wherein said lipid concentrate comprises, by weight about 15% cholesterol, about 10% lecithin and ceramides, and about 75% linoleic, Linolenic and arachidonic acids.

24. The composition of Claim 14 compressing the following constituents, by weight:

Isopropyl Myristate	about	5.0%
Cetyl Alcohol	about	3.0%
Arlacel 165	about	5.0%
Benzyl Alcohol	about	1.0%
Lipid Concentrate	about	10.0%
Vitamin E	about	1.0%
70% Sorbitol Solution	about	25.0%
Distilled Water	about	50.0%

25. The composition of Claim 24 wherein said lipid concentrate comprises, by weight about 30% cholesterol, about 20% lecithin and ceramides, and about 50% linoleic, linolenic and arachidonic acids.

26. The composition of Claim 14 wherein said lipid concentrate is present in a weight proportion of about 1% to about 50%.

INTERNATIONAL SEARCH REPORT

International Application No PCT/US89/03551

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC(4): A61K 31/685, 31/56, 31/20

U.S.Cl.: 514/77,78,171,558

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
U.S.	514/77,78,171,558

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category *	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
X	US, A 4,760 096 (SAKAI ET AL) 26 July 1988. See column 8, lines 1-30	1-26
X	N. Chemical Abstracts Vol. 93, Abstract No. 120270E, Moria et al., Jpn. Kokai Tokkyo Koho 80 33 451 08 March 1980.	1-26
X	N. Chemical Abstracts, Vol. 105, Abstract No. 66280J, Hanjani et al. Ger. Offen. DE 3 537 723 24 April 1986.	1-26
X	N. Chemical Abstracts Vol 106 Abstract No. 162393Q, Kaneko et al, Jpn. Kokai Tokkyo Koho JP 61,289,013 19 December 1986.	1-26

* Special categories of cited documents: [10]

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IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
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